SHORT REPORT

Vasculitic polyradiculopathy in systemic lupus erythematosus

Taresa L Stefurak, Gyl Midroni, Juan M Bilbao

Abstract

A 22 year old woman with recently diagnosed systemic lupus erythematosus presented with subacute progressive areflexic paraparesis, electrophysiologically identified as a pure axonal polyradiculopathy. Sural nerve biopsy disclosed necrotising vasculitis. A striking radiological feature was marked enhancement of the cauda equina with gadolinium.

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University of Toronto, Canada
T L Stefurak

Department of Neurology
G Midroni

Department of Pathology, St Michael's Hospital, 30 Bond Street, Toronto, Canada
J M Bilbao

Correspondence to:
Dr G Midroni, Neurophysiology laboratory, St. Michael's Hospital, 30 Bond Street, Toronto, Ontario, Canada M5B 1W8. Telephone 00416 864 5193; fax 00416 864 6095.

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An estimated 10%–20% of patients with systemic lupus erythematosus show peripheral nervous system involvement.[1 2] Disease of the peripheral nervous system most often presents as a sensorimotor polyneuropathy,[2 3] with less common syndromes including mononeuropathy multiplex or asymmetric polyneuropathies, and an acute[4 5] or chronic[6] demyelinating polyradiculopathy.

Documented peripheral nervous system pathology in associated with systemic lupus erythematosus polyneuropathies and asymmetric peripheral neuropathies includes nonspecific axonal and microvascular changes, as well as vasculitis.[2 3] Demyelination has consistently been indirectly implicated in polyradiculopathies associated with systemic lupus erythematosus,[4–6] but pathological verification is very limited. We describe a patient with systemic lupus erythematosus and a subacutely evolving axonal polyradiculopathy in which vasculitis was likely to be the pathogenic mechanism. The unusually morbid clinical course offers additional insight into the pathology of peripheral nervous system involvement in systemic lupus erythematosus, and highlights the importance of MRI, electrodiagnostic testing, and nerve biopsy in defining a diagnosis.

Case report

A 22 year old woman from Djibouti presented with fatigue, rash, arthralgias, and severe lower back and thigh pain. She did not have sicca symptoms. Initial examination disclosed a fine maculopapular rash on her legs, and active oligoarticular arthritis. Although she complained of leg weakness, only minimal bilateral proximal leg weakness was found on examination. Early laboratory findings were notable for anaemia (Hb 111 g/l), leukopenia (White blood cells 3.2×10^6/l), increased erythrocyte sedimentation rate (96 Westergren), raised antinuclear antibodies (1:320 homogenous), and low complement (C3 0.44 g/l, C4<0.1 g/l; normal >0.9 g/l, >0.16 g/l respectively). With this initial presentation she met formal ARA diagnostic criteria for systemic lupus erythematosus, and was started on 20 mg prednisone daily.

Over the next 3 months she experienced increasing leg and low back pain and progressive weakness. In hospital, initial neurological examination showed normal arm strength, with grade 3–4 (MRC) weakness in the proximal left leg muscles and in left foot dorsiflexion, with milder proximal right leg weakness. Reflexes were normal in the arms but reduced in the legs, and no sensory deficits were found.

An electrodiagnostic examination showed findings diagnostic of multiple bilateral lumbosacral radiculopathies. Motor amplitudes were markedly reduced to <25% of the lower limit of normal in the legs with excellent sensory responses (sural nerve 13 μV; superficial peroneal nerve 54 μV). Distal latencies, F latencies, and conduction velocities were all normal, and no conduction block or temporal dispersion was seen at any site (four motor nerves tested). Fibrillation potentials were present in multiple proximal and distal leg and paraspinal muscles spanning the left L4-S1 myotomes, maximal at L5. Conduction studies and needle examination of the arms were normal.

T1 weighted MRI of the cauda equina showed marked contrast enhancement of the lumbosacral nerve roots (fig 1 A, B, C). T2 weighted images were normal. Examination of CSF performed on three occasions showed raised protein (0.77 to 1.05 g/l). CSF cell counts, glucose, cultures, and cytology were repeatedly normal. Other investigations during the hospital stay included normal creatine kinase, venereal disease research laboratory test, HIV serology, serum angiotensin converting enzyme (ACE), and serum immunoelectrophoresis. Anti-dsDNA and antineutrophil cytoplasm antibodies (ANCAs) were negative, but anti-Ro (SSA) antibodies were strongly positive. Gallium scan, chest radiography,

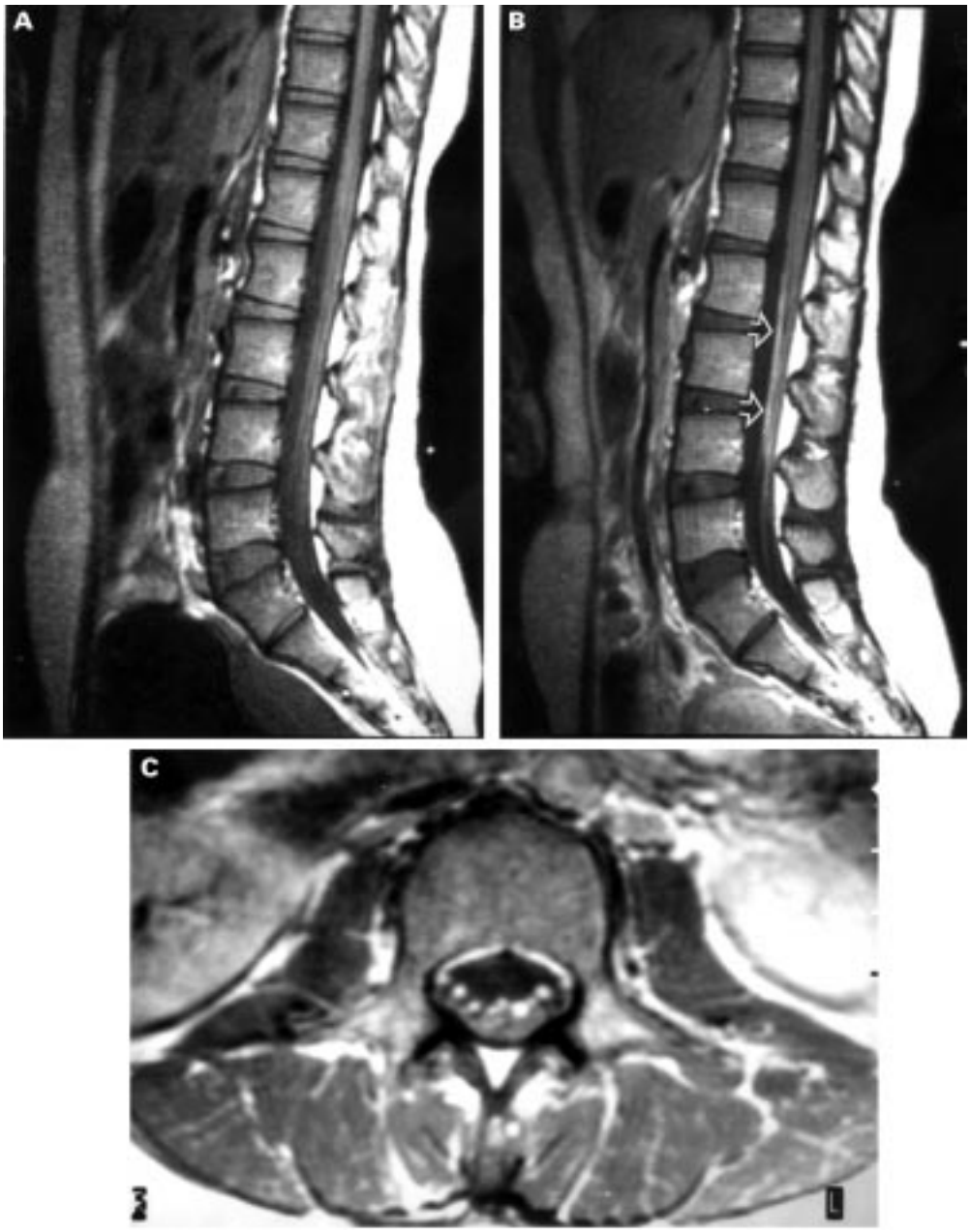

Figure 1 MRI of lumbar spine: sagittal T1 weighted images before (A) and after (B) gadolinium show enhancement of a nerve root along its entire length (arrowheads). Axial T1 weighted gadolinium enhanced images at the L4/L5 level (C) show multiple enhancing nerve roots in cross section.

abdominal ultrasound, and bone marrow examination were normal.

Her leg weakness and back pain continued to worsen despite treatment with oral prednisone (1.5 g/kg daily), intravenous immune globulin (0.4 g/kg daily for 5 days), and pulse corticosteroids (1 g methylprednisolone given intravenously daily for 3 days). After 10 days of treatment she left the hospital against medical advice taking 1 mg/kg prednisone, but was readmitted 2 weeks later. Examination 1 month after the initial neurological assessment showed complete paralysis of both legs, with grade 3–4 MRC bilateral arm weakness, severe weakness of neck flexion, but no cranial nerve involvement. All deep tendon reflexes were absent, but there were still no significant sensory deficits. Repeat electrodiagnostic examination, 6 weeks after the initial study, showed marked progression of her polyradiculopathy with absent motor responses in the legs, low motor amplitudes in the arms, but preserved sensory responses. There were still no electrophysiological features of demyelination. Fibrillation potentials were now present in the arm and cervical paraspinal muscles. Nerve and muscle biopsy disclosed necrotising vasculitis in nerve and muscle (fig 2), but no significant ongoing Wallerian degeneration in the sural nerve.

The patient finally stabilised (no further progression of weakness, resolution of back and leg pain) 8 weeks after her initial neurological assessment on a combination of corticosteroids (1 g methylprednisolone intravenously for 5 days, then 100 mg/day for 10

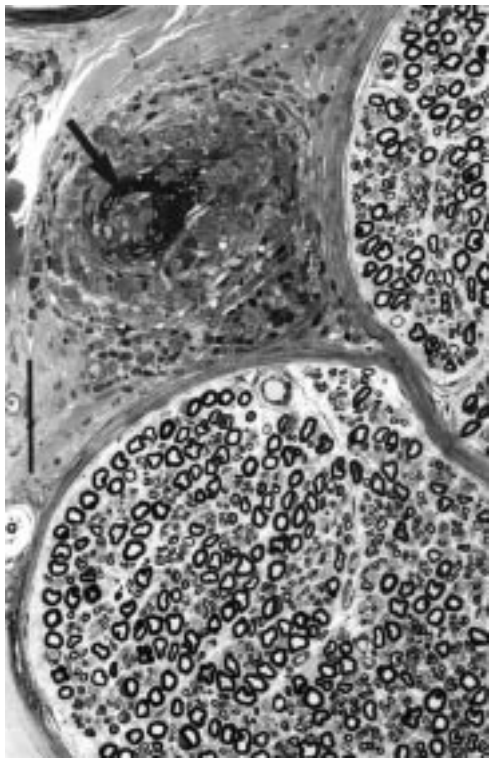

Figure 2 Sural nerve biopsy specimen (plastic embedded, stained with toluidine blue, bar=0.1 mm): Epineurial arteriole shows dense inflammatory cell infiltrate with fibrinoid necrosis (arrow). Note sparing of myelinated fibre population.

days, then 1 mg/kg prednisone, cyclophophamide (500 mg/m^2 infusion, followed by 2.5 mg/kg oral daily dose), and plasma exchange (5 exchanges over 9 days). She was discharged to rehabilitation on 1mg/kg prednisone and 2.5 mg/kg cyclophosphamide. Over the subsequent year she has improved very slowly with a proximal-distal evolution. At 1 year after clinical stabilisation, arm strength has normalised. Strength is grade 4 (MRC) in hip flexion, adduction, and abduction, grade 3–4 MRC in knee extension and flexion, and grade 1–2 MRC in foot dorsiflexion and plantarflexion. She can walk with a cane.

Discussion

The most common peripheral nerve syndrome seen in systemic lupus erythematosus is a mild to moderately severe symmetric sensorimotor polyneuropathy, usually with a predominant sensory component.[1–3] Nerve biopsy in this setting usually shows axonal degeneration or axonal depletion, often accompanied by non-specific vascular changes or chronic perivascular inflammation.[2 3] Less often biopsy may show necrotising vasculitis.[3] Asymmetric or multifocal neuropathies are less common in systemic lupus erythematosus, with vasculitis often suspected and sometimes demonstrated.[2 3]

A clinical picture of proximal and distal weakness, areflexia, and increased CSF protein (a polyradiculopathy), evolving either acutely[4 5] or chronically[6–8] has also been well documented. Electrophysiological studies and the patients' clinical course have consistently implicated demyelination as an important pathophysiological element.[4–6] However, the pathology of this clinical syndrome is unclear, as available information comes from necropsy study or nerve biopsy performed before the availability of modern techniques for the accurate study of myelin and axon pathology.[7–9]

Our patient showed a number of unique clinical and laboratory features, some not previously described in systemic lupus erythematosus.

Her disability was caused by an axonal, purely motor, polyradiculopathy. All electrophysiological findings indicated an axonal lesion at the ventral roots. Her very slow recovery has also been in keeping with axonal regeneration rather than remyelination, as contrasted with the rapid recoveries made by most of the previously reported patients with a demyelinating polyradiculoneuropathy.[5 6 8]

Nerve biopsy (fig 2) showed necrotising vasculitis, which we postulate was the cause of the patient's axonal polyradiculopathy. It may be argued that her clinical syndrome was due to the cooccurrence of vasculitis and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). However, clinically this patient would be extremely atypical for CIDP in her fulminant course with complete denervation of the lower limbs, in her excruciating leg and back pain, and in her very slow length dependent recovery. Reflexes were relatively preserved until severe generalised weakness was present, and her facial nerve was not affected clinically—also atypical for severe CIDP. She was unusually resistant to a treatment regimen usually very effective in CIDP. On laboratory testing we found no electrophysiological features of demyelination on two extensive electrodiagnostic studies done 6 weeks apart, and nerve biopsy also failed to show demyelination; CIDP therefore seems very unlikely. Although vasculitis has been amply described in peripheral nerve disease associated with systemic lupus erythematosus,[2 3] this pathological finding has been documented only once previously in systemic lupus erythematosus polyradiculopathy (in a necropsy specimen)[9]—this patient too had a motor dominant polyradiculopathy.

In our patient, the pathological site was defined at an early clinical stage by gadolinium enhancement of the cauda equina on MRI. Such enhancement is a non-specific finding which has previously been documented in Guillain-Barré syndrome, CIDP, meningeal carcinomatosis, infectious polyradiculitis, arachnoiditis, and sarcoidsois.[10] Nerve root enhancement has not previously been reported either in systemic lupus erythematosus associated, or in vasculitic, polyradiculopathy. Enhancement results from an impaired blood-nerve barrier, but it cannot be established whether in our patient this occurred as a primary pathophysiological element of the peripheral nerve disease, or secondary to the axonal degeneration.

This patient's peripheral nerve disease was unusually aggressive. The patient progressed despite the use of high dose steroids, usually

effective in treating neurological manifestations of systemic lupus erythematosus.[1] Although we cannot be certain what component of her treatment was most important, the introduction of intravenous cyclophosphamide pulses seemed to be important in stabilising her clinical situation, as has been found by others treating severe vasculitic neuropathies related to systemic lupus erythematosus.[11 12]

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